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TELEFAX

Date: January 23, 2006 Total pages: 19 including cover
To: US PTO Telephone: Telefax: 517-273-8300
From: Rivka Monheit Telephone: 404-879-2152 Telefax: (404) 879-2160
Our Docket No. MIT 5261 Client/Matter No. 701350/00048
Your Docket No.

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MESSAGE:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant: Paul R. Schimmel
Serial No.: 08/249,689 Art Unit: 1631
Filed: May 26, 1994 Examiner: John S. Brusca
For: *DESIGNING COMPOUNDS SPECIFICALLY INHIBITING RIBONUCLEIC
ACID FUNCTION*

Attachments:

Transmittal Form PTO/SB/21
Fee Transmittal Form PTO/SB/17
Reply to Response to Remand by the Board of Patent Appeals
Copy of Response to Remand mailed on December 23, 2005

{45063796.1}

PTO/SB/21 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	08/249,689	
	Filing Date	May 26, 1994	
	First Named Inventor	Paul R. Schimmel	
	Art Unit	1631	
	Examiner Name	John S. Brusca	
Total Number of Pages in This Submission	19	Attorney Docket Number	MIT 5261

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ENCLOSURES (Check all that apply)		
<input checked="" type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input checked="" type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Copy of Examiner's Response to Remand mailed on December 23, 2005
Remarks _____		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Pabst Patent Group LLP		
Signature	<i>Rivka D. Monheit</i>		
Printed name	Rivka D. Monheit		
Date	January 23, 2006	Reg. No.	48,731

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:			
Signature	<i>Carla Stone</i>		
Typed or printed name	Carla Stone	Date	January 23, 2006

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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PTO/SB/17 (12-04)

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Effective on 12/09/2004.

Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL
For FY 2005☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$) 0.00

Complete if Known

Application Number	08/249.689
Filing Date	May 26, 1994
First Named Inventor	Paul R. Schimmel
Examiner Name	1631
Art Unit	John S. Brusca
Attorney Docket No.	MIT 5261

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METHOD OF PAYMENT (check all that apply)
☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____

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For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

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FEE CALCULATION**1. BASIC FILING, SEARCH, AND EXAMINATION FEES**

Application Type	FILING FEES		SEARCH FEES		EXAMINATION FEES		Fees Paid (\$)
	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee (\$)	Small Entity Fee (\$)
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50	25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200	100
Multiple dependent claims	360	180

Total Claims	Extra Claims	Fee (\$)	Fee Paid (\$)	Multiple Dependent Claims	Fee (\$)	Fee Paid (\$)
- 20 or HP = 0	x	=				

HP = highest number of total claims paid for, if greater than 20

Indep. Claims	Extra Claims	Fee (\$)	Fee Paid (\$)
- 3 or HP = 0	x	=	

HP = highest number of independent claims paid for, if greater than 3

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee (\$)	Fee Paid (\$)
- 100 =	/ 50 =	(round up to a whole number) x	=	

4. OTHER FEE(\$)

Non-English Specification, \$130 fee (no small entity discount)

Other: _____

SUBMITTED BY

Signature	<i>Rivka D. Monheit</i>	Registration No. (Attorney/Agent)	48,731	Telephone	(404) 879-2152
Name (Print/Type)	Rivka D. Monheit	Date	January 23, 2006		

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant: Paul R. Schimmel

**RECEIVED
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Serial No.: 08/249,689

Art Unit: 1631

JAN 23 2006

Filed: May 26, 1994

Examiner: John S. Brusca

For: *"DESIGNING COMPOUNDS SPECIFICALLY INHIBITING RIBONUCLEIC
ACID FUNCTION"*Assistant Commissioner for Patents
Washington, D.C. 20231**REPLY TO RESPONSE TO REMAND
BY THE BOARD OF PATENT APPEALS**

Sir:

Although it does not appear that the appellant is given any right to reply to the Group's Request for Rehearing, or the Response to Remand mailed December 23, 2005¹, and that there are apparently no time limits for action at this stage, it is believed that the Board, in the interest of fairness, will consider remarks by the appellant.

This case has now been heard, and decided, by the Board of Appeals twice. The second decision was rendered almost two and one half years ago. Since the Group did not like the decision, it waited a year to request rehearing. A second delay of almost five months followed the remand. Since a terminal disclaimer has been filed in this application, the patent term is running regardless of the outcome of this appeal. None of the method claims are in issue, all

¹ A copy of the Response to Remand, dated December 23, 2005, is enclosed since PAIR does not indicate that a copy was sent to the Board.

U.S.S.N. 08/249,689

Filed: May 26, 1994

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BY THE BOARD OF PATENT APPEALS**

having been allowed. It would be greatly appreciated if this case would be considered quickly, although it is understood that the case is complicated, and the Board always does a very thorough and careful review.

This was an appeal from the rejection of claims 11-13, 17-19, and 21 in the Office Action mailed January 11, 2002, in the above-identified patent application, and maintained in the Advisory Action mailed June 10, 2002. A decision by the Board of Appeal was rendered October 30, 2005.

The claims are directed to a method for designing a compound that specifically inhibits a targeted ribonucleic acid function (claims 1, 3-10, 14-16, and 20) (all allowed and not in issue on appeal), and the compound identified by the method, as amended following the decision by the Board dated October 30, 2003, to be specific to the minor groove of the acceptor stem of a tRNA (claims 11, 13, 18, 19, and 21).

It appears that the Examiner's argument is that the sequence and structure of the compound are unknown, therefore one would not be able to envision a compound which is complementary to this sequence and structure, and the requirement under 35 U.S.C. 112, written description is not met. This is factually incorrect.

The original claim 11 on appeal was much broader than the claim now before the Board. This is limited to a compound which is defined by its function and its structure, since it must be complementary to the site on the minor groove of the acceptor stem of a tRNA to be inhibited, and must contain hydrogen bond donor and acceptor sites arranged to specifically bind and inhibit the function of the targeted RNA molecule. The RNA is now limited to (1) the minor

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groove of (2) a tRNA acceptor stem. The figures, specification, and numerous prior art references cited throughout the prosecution amply demonstrate that well before this application was filed, the primary, secondary and tertiary structures of the tRNAs, including the acceptor stems, were well known. This is further demonstrated by the examples which demonstrate the identification of the criticality of compounds which bind to the minor groove of the acceptor stem of the tRNA to inhibit their function. Example 4 shows how modification of the structure through substitution of a single base can be used to inhibit transcription, thereby inhibiting function of the tRNA. Well known, routine methods for making compounds complementary to the primary, secondary and tertiary structure of this critical region within the minor groove of the acceptor stem of the tRNA are described at pages 37-39. The declarations submitted during prosecution further demonstrate that once one had this structure, it was routine to make complementary compounds to the structure.

In summary, the application discloses providing compounds which are complementary to the minor groove of tRNA acceptor stems. The primary, secondary and tertiary structures of the tRNAs were well known at the time of filing. Computer programs were commercially available into which one could put the primary structure of the tRNA molecules to provide a model of the site to which the complementary molecule would bind, and thereby know its secondary and tertiary structure, and from this information, the structure and function of a molecule complementary and binding to this site.

This information clearly meets the requirements under 35 U.S.C. 112, written description which the Board articulates so well in its decision to Remand beginning at page 5. There is no

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need to repeat this analysis. The previous decision by the Board was correct and the request for rehearing should be denied.

The examiner argues on page 3 that if you have the structure of the key, you do not have the structure of the lock. It is difficult to know how to respond to this argument. We agree that the present situation is analogous, although it would be better to state that appellant has provided the lock, and that one would know the shape of the key from the lock. This is, of course, exactly what a locksmith does when someone loses their key - he inserts into the lock a special apparatus that when turned, has small bars that move in or out as necessary to conform to the spaces within the lock. When this is removed, one has the shape of the key. The converse is also true, for anyone who has ever had all of their locks changed to fit a single key. Once one has either shape, you have the other.

The examiner spends much time arguing that in contrast to antibodies, whose general shape and structure is known, the claimed compounds are undefined in structure because they are only defined by their complementarity to some equally undefined target. This is nonsense - the claims as limited after the Board's decision are restricted to those binding the minor groove of the acceptor stem of tRNAs, compounds who were extremely well characterized as to their primary, secondary, and tertiary structures long before appellant filed his application.

The examiner also argues that appellant has only provided information on compounds which bind to the minor groove of the acceptor stem of a tRNA, not proven function. Of course, that is exactly what example 4 proves - once the shape within the minor groove is altered, the tRNA is unable to function as a tRNA because the enzyme is no longer able to move freely along

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the minor groove - and as example 4 shows, only one minor change, that of one group of one nucleotide within this critical region is required to inhibit function.

The Board requested the examiner's comments regarding the declarations under 37 C.F.R. 1.132 but it does not appear there is any analysis, other than to copy into the response the requirements for when the examiner should consider opinion evidence.

Refusal of the Request for Rehearing by the Board of Patent Appeals and Interferences is earnestly solicited.

A handwritten signature in black ink, consisting of a large, stylized capital 'P' followed by a horizontal line extending to the right.

Patrea L. Pabst
Reg. No. 31,284

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/249,689	05/26/1994	PAUL R. SCHIMMEL	MIT5261	9517

23579 7590 12/23/2005

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DEC 27 2005

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EXAMINER

BRUSCA, JOHN S

ART UNIT PAPER NUMBER

1671

DATE MAILED: 12/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Application/Control Number: 08/249,689

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Art Unit: 1631

Response to Remand to Examiner in Application No. 08/249689 by the Board of Patent Appeals and Interferences, mail date 19 September 2005

The Board of Patent Appeals and Interferences issued a remand in this application to the examiner after consideration of a request for rehearing of the decision by the Board, mail date 30 October 2003. In the Board decision, a rejection under 35 U.S.C. § 112, first paragraph for lack of written description was reversed concerning claims drawn to products that bind the minor groove of the acceptor stem of tRNA and inhibit the function of the tRNA. In the remand the Board requested additional discussion of issues of record. In particular the Board requested a comparison of the facts of the instant application with that of *Univ. of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (CAFC 2004).

It is noted that the Remand filed by the Board on 19 September 2005 does not reflect the amendment entered 24 December 2003 in which claims 12 and 17 were cancelled and claims 11, 18, and 19 were amended. The pending claims rejected for lack of written description are 11, 13, 18, 19, and 21.

In an attempt to thoroughly respond to the issues discussed in the remand, the application file has been reviewed. Detailed below are clarifications of several points made by the Office during prosecution of the instant application.

35 U.S.C. 112, first paragraph states that "The specification shall contain a written description of the invention." This requirement cannot be satisfied by showing that post filing art describes the invention, or that the specification enables to make and use the invention.

On page 3 of the appeal brief filed 16 September 2002 the appellants noted a reduction to practice on pages 31-33 and page 36, however the sections pointed to merely show that

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mutations in the stem region of a tRNA inhibit the function of the tRNA molecules. The section pointed to therefore shows a possible critical region in a functional tRNA that could be targeted by a compound, but does not reduce to practice the claimed compounds. That is, there is no written description of any chemical structure(s) which have the function of being inhibitory to the targeted critical region.

The declarations of Julius Rebek Jr. and James R. Williamson filed 11 April 2002 discuss the minor groove of tRNA. The declarations discuss possible interactions with a hypothetical compound that binds a minor groove of tRNA including hydrophobic interactions, hydrogen bonds, electrostatic interactions, and steric constraints. The declarations discuss methods of computer modeling of hypothetical compounds that could bind to a minor groove of tRNA. The declarations analogize design of the claimed compounds with a lock and key, however, as previously noted in the Examiner's Answer mailed 02 January 2003, design of locks and keys are different than design of chemical compounds. If the analogy must be pursued, however, then the instant claims are analogous to an application that claims a lock (comprising mechanically complicated structures), but only describes a key. Description of a key does not describe the details of a lock with which the key interacts. The Williamson declaration discusses compounds that bind the minor groove of DNA and a ribosomal protein that binds to ribosomal RNA but does not discuss examples of compounds that bind to tRNA. It is noted that the claimed compounds do not merely bind to a critical site, but must also inhibit the function of a tRNA. Neither declaration addresses the limitation of inhibition of function of a tRNA in their discussion of design of the claimed compounds. The declarations do not present any objective evidence that the instant specification describes the claimed compounds. The evidence presented

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in the declarations is relevant to whether one of skill in the art would be enabled to make and use a compound that binds to the minor groove of a tRNA, rather than whether the claimed compounds are described. It is noted that both declarations express a legal opinion that the claimed compounds are described, but as noted below, the MPEP states at 716.01(b) that opinion evidence is not given any weight.

OPINION EVIDENCE

Although factual evidence is preferable to opinion testimony, such testimony is entitled to consideration and some weight so long as the opinion is not on the ultimate legal conclusion at issue. While an opinion as to a legal conclusion is not entitled to any weight, the underlying basis for the opinion may be persuasive. In *re Chilowsky*, 306 F.2d 908, 134 USPQ 515 (CCPA 1962) (expert opinion that an application meets the requirements of 35 U.S.C. 112 is not entitled to any weight; however, facts supporting a basis for deciding that the specification complies with 35 U.S.C. 112 are entitled to some weight); In *re Lindell*, 385 F.2d 453, 155 USPQ 521 (CCPA 1967) (Although an affiant's or declarant's opinion on the ultimate legal issue is not evidence in the case, "some weight ought to be given to a persuasively supported statement of one skilled in the art on what was not obvious to him." 385 F.2d at 456, 155 USPQ at 524 (emphasis in original)). In assessing the probative value of an expert opinion, the examiner must consider the nature of the matter sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986). See also In *re Oelrich*, 579 F.2d 86, 198 USPQ 210 (CCPA 1978) (factually based expert opinions on the level of ordinary skill in the art were sufficient to rebut the prima facie case of obviousness); *Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989) (statement in publication dismissing the "preliminary identification of a human b-NGF-like molecule" in the prior art, even if considered to be an expert opinion, was inadequate to overcome the rejection based on that prior art because there was no factual evidence supporting the statement); In *re Carroll*, 601 F.2d 1184, 202 USPQ 571 (CCPA 1979) (expert opinion on what the prior art taught, supported by documentary evidence and formulated prior to the making of the claimed invention, received considerable deference); In *re Beattie*, 974 F.2d 1309, 24 USPQ2d 1040 (Fed. Cir. 1992) (declarations of seven

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persons skilled in the art offering opinion evidence praising the merits of the claimed invention were found to have little value because of a lack of factual support); Ex parte George, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991) (conclusory statements that results were "unexpected," unsupported by objective factual evidence, were considered but were not found to be of substantial evidentiary value).

On page 7 of the appellant's reply brief filed 03 March 2003 the appellants state that the structure of the claimed compounds are defined by their interactions with the target site on the stem of tRNA. However the claims are drawn to compounds that are functionally defined by the ability to bind to the minor groove of the acceptor stem of a tRNA in claims 11, 13, and further limited to a target of tRNA^{Ala} in claim 18, a target of G3:U70 in the stem in claim 19, and a compound that is a nucleic acid in claim 21. It is further noted that the genus of critical sites that allows for inhibition of tRNA function when bound by the claimed compounds of claims 1, 13, 18, and 21 is not described. Although conserved structures of tRNA acceptor stems are described, there is no description of which sites in the acceptor stem allow for inhibition of function when bound by the claimed compound. Claim 19 is limited to one site of an acceptor stem, however the specification only shows that mutations in the site of claim 19 results in inhibition of tRNA function, which does not equate to a description of a wild type site that inhibits tRNA function when bound by the compound of claim 19. The appellants do not explain how knowledge of a binding site on a target leads to description of the structure of a compound that binds the target. Although a binding site comprises a number of chemical groups that can form hydrogen bonds, hydrophobic interactions, electrostatic interactions, and further provides steric constraints to a compound that binds the binding site, these constraints provide little correlation with the overall structure of a compound that binds the binding site. Many polar chemical groups in a compound can form hydrogen bonds, many nonpolar chemical groups can

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form hydrophobic interactions, many charged chemical groups can form electrostatic interactions, and many compounds are able to fit within the steric constraints of the binding site. What is missing from the description is the structure of a compound that combines and properly orients the chemical groups required to bind the minor groove of a tRNA acceptor stem and inhibit the function of the tRNA. The Board noted this point in their decision mailed 30 October 2003 in the instant application (regarding claims 11-13 and 21 prior to the amendment of 24 December 2003 in which claims were limited to a target of tRNA acceptor stem) as follows:

Appellant argues that the hydrogen bond donor and acceptor sites are structural features tied to function, but merely stating that an unspecified compound has an arrangement of hydrogen bond donor and acceptor sites that allows the compound to bind a critical site in the minor groove of an unspecified RNA target molecule and inhibit RNA function does nothing to allow one skilled in the art to visualize or recognize the identity of the members of the genus. It may define a desirable result, but it does not define the inhibitor that achieves that result. That the "lock and key" mechanism of RNA inhibition may be analogous to the mechanism of antibody-antigen recognition is beside the point.

The Board's reasoning is equally applicable to a binding site that is limited to a tRNA acceptor stem. The only aspect of the claimed compounds that is described is the function of binding to the claimed binding site. The description of the claimed compounds ends at the interface of the binding site and the claimed compounds.

Compounds whose structure is not described may instead be described by other physical characteristics and by a known relation between a described function and structure. Antibodies that specifically bind an antigen may be described by description of the antigen in view of the relationship between the structure of an antigen and an antibody to which it binds. The structure of an antigen not only determines aspects of the binding pocket of its corresponding antibody,

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but possession of an antigen allows for assured possession of its corresponding antibody through well recognized methods of obtaining the corresponding antibody without requiring knowledge of the structure of the antibody. In *Noelle v. Lederman* 69 USPQ2d 1508 (CAFC 2004), the CAFC ruled that an antibody to human CD40CR antigen was not adequately described in an application for which priority was claimed because the claimed application did not adequately describe the human antigen. Instead, the claimed application described only mouse CD40CR antigen. The CAFC stated that if the human antigen had been described in the claimed application, then the antibody to the human antigen would also have been adequately described.

In pages 19-23 of the appellant's brief filed 16 September 2002 the appellants analogize written description of antigens and antibodies to that of the claimed invention. The appellants state that the critical region of the RNA is analogous to an isolated and described antigen, and the claimed compounds are analogous to an antibody that binds a described antigen. The analogy is inaccurate because although some constraints on the structure of the claimed compound are imposed by the critical site on the tRNA to which it binds, the claimed compound does not have a recognized conserved structure, nor is there a method of obtaining the claimed compound that is so direct and recognized that possession of the critical site equates to possession of the claimed compound. The only method of obtaining the claimed compound described is by the method of step (e) of instant claim 1, which although enabled, requires considerable trial and error computational experimentation with unpredictable results. There is no known or disclosed correlation between the claimed function of the claimed compounds and their structure.

In pages 6-7 of the Remand mailed 19 September 2005, the Board notes Example 16 of the USPTO Synopsis of Application of Written Description Guidelines which deals with written

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description of antibodies that specifically bind a described antigen. The example states a number of reasons why the antibody should be considered as described. The reasons are contrasted with the instant facts as follows:

1) There is a routine art-recognized method of making antibodies to fully characterized antigens. In contrast although there is a prior art method of designing compounds that bind to a target molecule, there is no prior art method of making the specifically claimed compounds.

2) There are well-defined structural characteristics for the five classes of antibody. In contrast there are no examples of the claimed compounds in the instant specification or the prior art.

3) The functional characteristics of antibody binding. It is assumed that this refers to the conserved structural-functional properties of antibody binding sites. In contrast the claimed compounds are defined only functionally by their ability to bind to a critical site and inhibit function of a tRNA.

4) Antibody technology is well developed and mature. In contrast the methods of making the claimed compounds requires computational experimentation to design compounds with unpredictable results, and further would require experimental testing to determine if proposed structures inhibit the function of a tRNA molecule.

In *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (CAFC 2004) the CAFC ruled that claims drawn to methods of using a COX-2 inhibitor were not described in view of a description of a screening method for COX-2 inhibitors and the absence of description of the inhibitors themselves. COX-2 is an enzyme known as a cyclooxygenase whose metabolic products result in inflammation. Regarding description in different fact situations, the CAFC

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contrasts description of polynucleotides and description of the general class of chemical compounds at page 1894:

We agree with Rochester that *Fiers*, *Lilly*, and *Enzo* differ from this case in that they all related to genetic material whereas this case does not, but we find that distinction to be unhelpful to Rochester's position. It is irrelevant; the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue, in fact, where there might be some basis for finding a written description requirement to be satisfied in a genetics case based on the complementarity of a nucleic acid and, for example, a protein, that correspondence might be less clear in a non-genetic situation. In *Enzo*, we explained that functional descriptions of genetic material can, in some cases, meet the written description requirement if those functional characteristics are "coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." 323 F.3d at 964 (quoting from the PTO's *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement*, 66 Fed. Reg. 1099, 1106). DNA and RNA are each made up of just four building blocks that interact with each other in a highly predictable manner. Each of those building blocks, or "nucleotides," is characterized by a unique "base": In the case of DNA, the four nucleotides include the bases adenine, thymine, cytosine, and guanine; RNA also includes adenine, cytosine, and guanine, but contains the base uracil in place of thymine. Adenine on one strand of DNA binds, or "hybridizes," to thymine on the other; in RNA, adenine binds to uracil; and in either DNA or RNA, cytosine binds to guanine. Given the sequence of a single strand of DNA or RNA, it may therefore have become a routine matter to envision the precise sequence of a "complementary" strand that will bind to it. Therefore, disclosure of a DNA sequence might support a claim to the complementary molecules that can hybridize to it.

The same is not necessarily true in the chemical arts more generally. Even with the three-dimensional structures of enzymes such as COX-1 and COX-2 in hand, it may even now not be within the ordinary skill in the art to predict what compounds might bind to and inhibit them, let alone have been within the purview of one of ordinary skill in the art in the 1993-1995 period in which the applications that led to the '850 patent were filed. Rochester and its experts do not offer any persuasive evidence to the contrary. As the district court pointed out:

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Tellingly, ... what plaintiff's experts' [sic] do *not* say is that one of skill in the art would, from reading the patent, understand what compound or compounds—which, as the patent makes clear, are necessary to practice the claimed method—would be suitable, nor would one know how to find such a compound except through trial and error ...

Plaintiff's experts opine that a person of ordinary skill in the art would understand from reading the '850 patent what method is claimed, but it is clear from reading the patent that one critical aspect of the method—a compound that selectively inhibits PGHS-2 activity—was hypothetical, for it is clear that the inventors had neither possession nor knowledge of such a compound.

Univ. of Rochester, 249 F. Supp. 2d at 229

Thus the CAFC stated that chemical compounds generally require more description than merely binding specificity. Because University of Rochester concerns description of a claimed method of using a compound that binds to and inhibits an enzyme it is more relevant to the instant fact situation than the antigen-antibody situation discussed above.

In the response to the request for reconsideration filed by the appellants on 24 November 2004, the appellants state on page 14 that the claimed compounds could be obtained without undue experimentation, however the rejection is based not on an enablement standard, but rather on a written description standard. The appellants have not shown how the instant claimed compounds are any better described than the COX-2 inhibitors in Rochester.

In the remand filed by the Board 19 September 2005, the Board notes some differences between the fact situation of Rochester and the instant application. The Board correctly states that in Rochester a critical site was not shown. In Rochester the patent described a bioassay for screening compounds to determine if the compounds inhibited COX-2 activity. It is clear that for COX-2 inhibitors to inhibit the target enzyme, the inhibitor must bind a site in the enzyme.

In the Rochester decision, the CAFC did not state whether description of a binding site was relevant to description of COX-2 inhibitors. The CAFC focused on the lack of description of the

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structure of the inhibitors and the lack of a known correlation between function and structure. The CAFC did state that knowledge of the three-dimensional structure of the enzyme target would not likely serve to describe the inhibitors of the enzyme (see the passage quoted above). It is further noted that instant claims 11, 13, 18, and 21 are drawn to compounds that bind to a genus of critical sites that is not adequately described, because only the critical site of claim 19 is specifically described, and it is not apparent from the specification that even the critical site of claim 19 is an operative embodiment, as noted above. The Board notes the appellant's assertions and declarations that suggest that knowledge of the structure of the critical site of the tRNA equates with knowledge of the structure of the claimed compounds. As discussed above, knowledge of the structure of a binding site is merely a starting point on a research project to develop the claimed compounds. The declarations of Rebek and Williamson do not show that one skilled in the art would believe that appellant had possession of the claimed compounds based on knowledge of a binding site. Finally, the Board notes that even antibodies that bind a described antigen have unpredictable structures in their binding sites. Nevertheless, the CAFC has ruled in *Noelle* that description of the structure of an antigen is sufficient to describe the corresponding antibody that binds the antigen. The CAFC has not extended that logic to other fact situations, and in *Rochester* it is plain that the CAFC position is that without a known correlation between function and structure, a functional description of a chemical compound is presumed to be inadequate to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

John S. Brusca 22 December 2005

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